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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/073,060	02/12/2002	David Mu	38002-0024	2406

26633 7590 01/12/2007
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EXAMINER	
GIBBS, TERRA C	
ART UNIT	PAPER NUMBER
1635	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/12/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/073,060	MU ET AL.	
	Examiner	Art Unit	
	Terra C. Gibbs	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 October 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,9-12,14,22-24,33-35 and 39-82* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3, 9-12, 14, 22-24, 33-35, and 39-82* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *October 27, 2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is a response to Applicant's Amendment and Remarks filed October 27, 2006.

Claims 1, 9, 12, 22, 33, 45, 47, 52, 59, and 62 have been amended. New claims 65-82 are acknowledged.

Claims 1-3, 9-12, 14, 22-24, 33-35, and 39-82 are pending in the instant application.

Claims 1-3, 9-12, 14, 22-24, 33-35, and 39-82 have been examined on the merits.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Information Disclosure Statement

Applicant's information disclosure statement filed October 27, 2006 is acknowledged. The submission filed October 27, 2006 is in compliance with the provisions of 37 CFR §1.97. Accordingly, the Examiner has considered the information disclosure statement, and a signed copy is enclosed herewith.

Claim Rejections - 35 USC § 112

In the previous Office Action mailed July 27, 2006, claims 59-64 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the

invention. **This rejection is withdrawn** in view of Applicant's Arguments filed October 27, 2006. Specifically, the Examiner is withdrawing this rejection because it is agreed that those skilled in the art would reasonably be apprised of the terms "first indirect measure" and "second indirect measure".

In the previous Office Action mailed July 27, 2006, claims 1-3, 9-12, 14, 22-24, 33-35, 39-64 were rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. **This rejection is withdrawn** in view of Applicant's Arguments filed October 27, 2006. Specifically, the Examiner is withdrawing this rejection because it is agreed that mammalian hepsin genes were well known in the art at the time of filing of the instant application. Further, the Examiner would like to make of record that the instant claims are specifically drawn to mammalian hepsin since the claims are drawn to methods of diagnosing cancer in a mammal or methods of monitoring the efficacy of a therapeutic treatment regimen in a patient, where the term patient has not been defined in the instant specification, but has been defined according to CancerWEB's On-line Medical Dictionary (see attached).

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In the previous Office Action mailed July 27, 2006, claims 1-3, 9-11, 39, 40, 44, 45, and 49-64 were rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for diagnosing an ovarian cancer in a mammal *ex vivo*, or a method for monitoring the efficacy of an ovarian therapeutic

treatment regimen in a patient *ex vivo*, comprising measuring hepsin gene copy number, does not reasonably provide enablement for a method for diagnosing *any* cancer in a mammal *in vivo* or a method for monitoring the efficacy of *any* cancer *in vivo*, comprising measuring hepsin gene copy number. **This rejection is maintained** for the reasons of record set forth in the previous Office Action mailed July 27, 2006. **It is also noted that new claims 65-70 and 77-82 are included in this rejection.**

Response to Arguments

In response to this rejection, Applicants contend that the instant rejection has been obviated since each of the independent claims have been amended to clarify that the recited method steps are carried out *ex vivo*. For example, Applicants contend that each of the independent diagnostic method claims or methods of monitoring therapeutic treatment efficacy as now recited indicate that the biological subject is "obtained from" a region of the mammal suspected to be precancerous or cancerous.

First, this contention has been fully considered but is not found persuasive because recitation of the term "obtained from" in claims 1-3, 39, 44, and 49-61, is confusing as detailed in the 35 U.S.C. 112, second paragraph rejection below. Briefly, the claims have been amended to recite, "detecting and measuring the hepsin gene copy number in a biological subject **obtained from** a region of the mammal that is suspected to be precancerous or cancerous", "determining a hepsin gene copy number in a biological subject **obtained from** a region of the mammal which is suspected to be precancerous or cancerous", or "determining a first indirect measure of hepsin gene

copy number in a biological subject **obtained from** a region of the mammal that is suspected to be precancerous or cancerous". As it reads, the claims are confusing because it appears that Applicants are claiming that the biological subject is **obtained from** a region of the mammal, which, logically, does not make sense.

Second, the rejection is maintained against claims 1, 3, 9-11, 39, 40, 44, 45, and 49-53, and 55-64 because the scope of the invention is so broad to include methods of diagnosing *any* cancer in a mammal or methods for monitoring the efficacy of *any* therapeutic treatment regimen in a patient, comprising measuring hepsin gene copy number where instant specification teaches that the hepsin gene copy number is not amplified in prostate tumor. For example, the instant specification at page 65, line 6 discloses, "Hepsin gene was not amplified in the tested prostate tumor samples". Further, the scope of the invention is so broad to include breast and lung tumor where the instant specification, at Table 4, teaches that out of 33 lung tumor samples tested, only one overexpressed the hepsin gene copy number. Table 4 also teaches that out of 35 breast tumor samples tested, only one overexpressed the hepsin gene copy number. Thus, this data appears to lack any statistical significance. Furthermore, the state of the art is unpredictable and the lack of support from the specification and prior art for the ability of a such methods of diagnosis and monitoring therapeutic treatment efficacy *in vivo*, to have such far-reaching effects such as into the manifestation of any cancer, results in the invention being unpredictable in terms of its use as presently claimed. It is noted that because claims 1-3, 39, 44, 49-61 are confusing (as discussed above and as detailed in the 35 U.S.C. 112, second paragraph rejection below), it cannot be

determined whether these claims exclude *in vivo* applicability for enablement purposes. Considering the unpredictability surrounding the extrapolation of data from experiments using different tumor samples and different, undisclosed measures of significance, the skilled artisan would have to practice undue and unpredictable trial and error experimentation in order to practice the invention commensurate in scope with these claims. Therefore, the rejection is maintained.

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In the previous Office Action mailed July 27, 2006, claims 12, 14, 41, and 46 were rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. **This rejection is maintained** for the reasons of record set forth in the previous Office Action mailed July 27, 2006. **It is also noted that new claims 71 and 72 are included in this rejection.**

Response to Arguments

In response to this rejection, Applicants contend that the instant rejection has been obviated since each of the independent claims have been amended to clarify that the recited method steps are carried out *ex vivo*. For example, Applicants contend that the independent diagnostic method claim as now recited indicates that the biological subject is "obtained from" a region of the mammal suspected to be precancerous or cancerous.

First, this contention has been fully considered but is not found persuasive

because recitation of the term "obtained from" in claims 12, 14, 41, and 46, is confusing as detailed in the 35 U.S.C. 112, second paragraph rejection below. Briefly, the claims have been amended to recite, "measuring a test level of hepsin mRNA expression in a biological subject **obtained from** a region of the mammal that is suspected to be precancerous or cancerous". As it reads, the claims are confusing because it appears that Applicants are claiming that the biological subject is **obtained from** a region of the mammal, which, logically, does not make sense.

Second, the rejection is maintained against claims 12, 14, 41, and 46 because the scope of the invention is so broad to include methods of diagnosing a breast or lung cancer in a mammal, comprising measuring hepsin mRNA expression where instant specification teaches that out of 33 lung tumor samples tested, and out of 35 breast tumor samples tested, only one overexpressed the hepsin gene copy number in each tumor sample set. However, it is well known in the art that overexpression of gene copy is not correlated to overexpression of mRNA levels. For further explanation, see Yoshimoto et al., 1986 Japanese Journal of Cancer Research, Vol. 77, pages 540-545 (Applicant's reference A71 in the information disclosure statement filed November 4, 2002). Furthermore, the prior art teaches that hepsin mRNA is amplified (overexpressed) in ovarian and prostate tumor samples, but is silent regarding breast or lung tumor samples. Even further, the state of the art is unpredictable and the lack of support from the specification and prior art for the ability of a such methods of diagnosis *in vivo*, to have such far-reaching effects such as into the manifestation of breast or lung cancer, results in the invention being unpredictable in terms of its use as presently

claimed. It is noted that because claims 12, 14, 41, and 46 are confusing (as discussed above and as detailed in the 35 U.S.C. 112, second paragraph rejection below), it cannot be determined whether these claims exclude *in vivo* applicability for enablement purposes. Considering the unpredictability surrounding the extrapolation of data from experiments using different tumor samples and different, undisclosed measures of significance, the skilled artisan would have to practice undue and unpredictable trial and error experimentation in order to practice the invention as claimed as it relates to breast and lung cancer diagnosis.

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In the previous Office Action mailed July 27, 2006, claims 22-24, 33-35, 42, 43, 47, and 48 were rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for monitoring the efficacy of an ovarian or prostate therapeutic treatment regimen in a patient *ex vivo*, comprising measuring hepsin mRNA, or a method for monitoring the efficacy of an ovarian, prostate, or lung therapeutic treatment regimen in a patient *ex vivo*, comprising measuring hepsin protein, does not reasonably provide enablement for a method for monitoring the efficacy of *any* cancer *in vivo*, comprising measuring hepsin mRNA or hepsin protein. **This rejection is maintained** for the reasons of record set forth in the previous Office Action mailed July 27, 2006. **It is also noted that new claims 73-76 are included in this rejection.**

Response to Arguments

In response to this rejection, Applicants contend that the instant rejection has been obviated since each of the independent claims have been amended to clarify that the recited method steps are carried out *ex vivo*. For example, Applicants contend that each of the independent diagnostic method claims or methods of monitoring therapeutic treatment efficacy as now recited indicate that the biological subject is "obtained from" a region of the mammal suspected to be precancerous or cancerous.

First, this contention has been fully considered but is not found persuasive because recitation of the term "obtained from" in claims 33-35, 43, and 48, is confusing as detailed in the 35 U.S.C. 112, second paragraph rejection below. Briefly, the claims have been amended to recite, "detecting a test hepsin protein expression level by contacting a biological subject **obtained from** a region of the mammal that is suspected to be precancerous or cancerous". As it reads, the claims are confusing because it appears that Applicants are claiming that the biological subject is **obtained from** a region of the mammal, which, logically, does not make sense.

Second, the rejection is maintained against claims 22-24, 33-35, 42, 43, 47, and 48 because the scope of the invention is so broad to include methods for monitoring the efficacy of *any* therapeutic treatment regimen in a patient or a method for diagnosing a breast cancer in a mammal, comprising measuring hepsin mRNA or hepsin protein where the specification and prior art describe that hepsin mRNA is overexpressed in prostate and ovarian tumor tissues and hepsin protein is overexpressed in ovarian, lung, and prostate tumor samples. The specification teaches that out of 35 breast tumor

samples tested and 33 lung tumor samples tested, only one overexpressed the hepsin gene copy number in each tumor sample set. However, it is well known in the art that overexpression of gene copy is not correlated to overexpression of mRNA levels. For further explanation, see Yoshimoto et al., 1986 Japanese Journal of Cancer Research, Vol. 77, pages 540-545 (Applicant's reference A71 in the information disclosure statement filed November 4, 2002). While the specification and prior art describe hepsin mRNA or protein overexpression in tumor tissues from ovarian, lung, and prostate, a correlation to other cancers, including breast cancer is lacking. Furthermore, the state of the art is unpredictable and the lack of support from the specification and prior art for the ability of a such methods of diagnosis and monitoring therapeutic treatment efficacy *in vivo*, to have such far-reaching effects such as into the manifestation of any cancer, results in the invention being unpredictable in terms of its use as presently claimed. It is noted that because claims 33-35, 43, and 48 are confusing (as discussed above and as detailed in the 35 U.S.C. 112, second paragraph rejection below), it cannot be determined whether these claims exclude *in vivo* applicability for enablement purposes. Considering the unpredictability surrounding the extrapolation of data from experiments using different tumor samples and different, undisclosed measures of significance, the skilled artisan would have to practice undue and unpredictable trial and error experimentation in order to practice the invention commensurate in scope with these claims.

Applicant's Amendment necessitated the new grounds of rejection presented below:

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3, 39, 44, 49-61, 12, 14, 41, 46, 33-35, 43, 48, 67, 68, 71, 72, and 75-80 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 12, 33, 52, and 59 recites either "detecting and measuring the hepsin gene copy number in a biological subject **obtained from** a region of the mammal that is suspected to be precancerous or cancerous"; "determining a hepsin gene copy number in a biological subject **obtained from** a region of the mammal which is suspected to be precancerous or cancerous"; "determining a first indirect measure of hepsin gene copy number in a biological subject **obtained from** a region of the mammal that is suspected to be precancerous or cancerous"; "measuring a test level of hepsin mRNA expression in a biological subject **obtained from** a region of the mammal that is suspected to be precancerous or cancerous"; or "detecting a test hepsin protein expression level by contacting a biological subject **obtained from** a region of the mammal that is suspected to be precancerous or cancerous". Recitation of the term "obtained from" renders the claims indefinite because the claims are confusing because it appears that Applicants are claiming that the biological subject is **obtained from** a region of the mammal, which, logically, does not make sense. Replacement of the language "biological sample" would obviate the instant rejection since, by logic, a biological sample can be

obtained from a region of the mammal that is suspected to be precancerous or cancerous. It is noted that claims 2, 3, 39, 44, 49-51, 53-58, 60, 61, 14, 41, 46, 34, 35, 43, 48, 67, 68, 71, 72, and 75-80 are included in this rejection because of their dependency therein.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Terra C. Gibbs whose telephone number is 571-272-0758. The examiner can normally be reached on 9 am - 5 pm M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

tcg
January 5, 2007

SEAN McGARRY
PRIMARY EXAMINER
AU 1635